9-Aminoacridine Hydrochloride

CAS #134-50-9
Swiss CD-1 mice, at 0.0, 0.025, 0.05, and 0.1% in feed
James Lamb IV, NTP/NIEHS Project Officer,
Dushyant Gulati, Robin Mounce, Suzann Shaver, and Susan Russell,
Environmental Health Research and Testing
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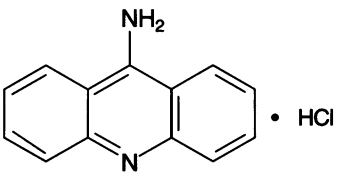

9-Aminoacridine hydrochloride (9AH), used as a topical antiseptic for humans, was tested for its effects on reproduction and fertility in Swiss CD-1 mice using the RACB protocol (Morrissey et al., Fundam Appl Toxicol 13:747–777 [1989]). Data from a 2-week dose-range-finding study (Task 1) were used to set exposure concentrations for the Task 2 continuous cohabitation study at 0.025, 0.05, and 0.1% in feed. Based on body weights and food consumption data, the estimated daily doses were approximately 31, 66, and 145 mg/kg.

One male and two female control mice, and one female in the middle dose group, died during the 18-week Task 2 cohabitation phase. While the male mice in the high dose group gained less weight than controls, only high dose female mean body weights were significantly lower by approximately 10% than control means during the study. While 9AH consumption did not alter the number of litters per pair, the number of pups per litter or their viability, the pup weight adjusted for body weight was reduced by 9% in the high dose group. This pup weight reduction may be related to the reduced postpartum dam weights.

In the absence of changes in F_0 fertility parameters, Task 3 was not conducted and the last litters from the control, middle, and high dose groups were reared by their dams. Approximately two thirds of the pups in the high dose group died before postnatal day 14, and pup weight at all times until weaning was reduced by approximately 30%. Pup survival and weight gain in the middle dose group were not changed. The increased morbidity at the high dose left insufficient pups to evaluate for fertility effects. Thus, Task 4 was performed using controls and middle dose group mice.

During the Task 4 mating trial, 9AH had no effect on the number of pups per litter, or their viability or weight. Thus, there was no adverse reproductive effect noted in the second generation at 0.05% 9AH.

After the F_2 pups were delivered and evaluated, the F_1 adults were killed and necropsied. While female body weights at the middle dose were not changed, liver weight was increased by approximately 30%, and adjusted kidney weights were reduced by approximately 10%. For treated males, body weight was reduced by approximately 10%, while adjusted liver weight was increased by approximately 25%. Sperm indices at necropsy were unchanged, as was estrous cycle length.

Thus, 9-aminoacridine hydrochloride induced some developmental toxicity in the form of reduced F_1 pup weight at the same dose that also reduced dam weight and at doses greater than those that increased F_1 liver weight. No changes in other fertility indices were observed. These data suggest that for 9-aminoacridine hydrochloride the hepatic effects are greater than any reproductive effects. Developmental toxicity could not be separated from the general toxicity.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB86163128/AS**
Chemical: **9-Aminoacridine Hydrochloride**
CAS#: **134-50-9**
Mode of exposure: **Feed**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	0.025%	0.05%	0.1%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	—, —	—, ↓
Kidney weight[a]	•	•	•
Liver weight[a]	•	•	•
Mortality	—, —	—, —	—, —
Feed consumption	—, —	—, —	—, —
Water consumption	•	•	•
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
x̄ litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, ↓
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight[a]	•	•	•
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•	•	•
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F_1 generation — Dose concentration →	•	0.05%	0.10%
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	•	—, —	↓, ↓
Mortality	•	—, —	↓, ↓
Adult body weight	•	↓, —	•
Kidney weight[a]	•	—, ↓	•
Liver weight[a]	•	↑, ↑	•
Feed consumption	•	—, —	•
Water consumption	•	•	•
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
Fertility index	•	—	•
# live pups/litter; pup wt./litter	•	—, —	•
Absolute testis, epididymis weight[a]	•	—, —	•
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	—, —	•
Epidid. sperm parameters (#, motility, morphology)	•	—, —, —	•
Estrous cycle length	•	—	•

Summary information	
Affected sex?	Both
Study confounders:	None
NOAEL reproductive toxicity:	0.05%
NOAEL general toxicity:	not determined
F_1 more sensitive than F_0?	Unknown
Postnatal toxicity:	Yes

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.